

WHAT IS CLAIMED IS

Claim 1. Apparatus for measuring reactions on a biochip during a microarray procedure by imaging the changes in height which occur at the spots of an array of spots on a biochip, said biochip including a transparent slide having a surface on which the spots are placed, said surface having a surface roughness of less than the height of molecules in the spots on said surface.

Claim 2. The apparatus of claim 1 in which the slide is transparent to electromagnetic radiation in a range of wavelengths used by said apparatus to form an image of the height profile of reactions at the spots of said array.

Claim 3. The apparatus of claim 1 including a prism having a first surface said surface having a surface roughness of less than about 300Å.

Claim 4. The apparatus of Claim 1 wherein said surface roughness is sufficiently lower to allow resolution of molecules in said spots.

Claim 5. The apparatus of Claim 1 wherein said surface roughness is lower than the change in height after a binding reaction.

Claim 6. A biochip including a transparent slide having a first surface, said surface having a surface roughness of less than about 300Å, said surface having thereon an array of spots, each of said spots including a biological test material.

Claim 7. A slide of transparent material said slide having first and second parallel planar surfaces, at least a first of said surfaces having a surface roughness of less than about 300Å.

Claim 8. An apparatus for measuring reactions on a biochip by imaging the changes in height of biomolecules which occur at the spots of an array of spots on the surface of the biochip comprising;

an optical imaging apparatus having a polarized light source emitting a polarized, extended beam of light;

a TIR structure having a TIR surface, the light from said polarized light source member being reflected only on a single time by the TIR surface, the array of spots being within the evanescent field associated with the total reflection at the TIR surface;

a polarization-sensitive, two-dimensional array detector, said detector detecting the light beam reflected from the TIR surface including the spatially distributed

polarization change caused by the array of spots;

the TIR surface having a surface roughness of less than the height of molecules in said spots.

Claim 9. An apparatus for imaging binding reactions on a biochip by imaging the changes in height of biomolecules which occur at the spots of an array of spots on the surface of the biochip comprising;

a TIR surface having a surface roughness sufficiently low that spots on the biochip can be resolved as separate images and that thickness changes can be resolved on the spots.

Claim 10. The apparatus of Claim 9 wherein said surface roughness is about 300Å or less within the measured area.

Claim 11. Apparatus for measuring reactions on a biochip by imaging the changes in height which occurs at the spots of an array spots on the surface of a biochip, said biochip including a transparent slide having a surface roughness sufficiently low to resolve as separate images changes in height in the femtogram/mm² range.

Claim 12. An apparatus for measuring binding reactions on a biochip by imaging the changes in height of biological material which occurs at the spots of an array of spots on the surface of the biochip wherein the surface roughness of said surface is a fraction of the biomolecule height.

Claim 13. An apparatus for measuring binding reactions on a biochip by imaging the changes in height of biological material due to the binding reactions which occur at the spots of an array of spots on the surface of the biochip wherein the surface roughness of said surface is sufficiently low to permit distinguishing the changes in height from the roughness features of the surface.

Claim 14. An apparatus for measuring reactions on a biochip by imaging the changes in height of biological material which occurs at the spots of an array of spots on the surface of the biochip comprising;

an optical imaging apparatus having a polarized light source emitting a polarized, extended beam of light;

a TIR structure having a TIR surface, the light from said polarized light source

member being reflected only on a single time by the TIR surface, the array of spots being within the evanescent field associated with the total reflection at the TIR surface;

a polarization-sensitive, two-dimensional array detector, said detector detecting the light beam reflected from the TIR surface including the spatially distributed

5 polarization change caused by the array of spots;

the TIR surface having a surface roughness that is sufficiently low to permit distinguishing the changes in height from the surface roughness features.

Claim 15. Apparatus for spatially resolved imaging of a plurality of spots in a bioarray of spots on the surface of a biochip comprising;

10 an optical assembly in which the biochip is a part and in which the surface is a TIR surface for an extended beam of polarized light introduced into the optical assembly, the said surface being the only TIR surface in the path of the beam of light;

a source of an extended beam of polarized light positioned in relation to the optical assembly to cause the extended beam of polarized light to enter the optical
15 assembly and to have a single total internal reflection in the optical assembly which total internal reflection occurs at the TIR surface, and thereafter to exit the optical assembly;

Claim 16. The apparatus of claim 15 further comprising an image capturing device positioned to receive the beam of light exiting from the optical assembly to record the spatially resolved changes in polarization impressed on the beam of light by the
20 plurality of spots of the bioarray which are within the area of the beam of light.

Claim 17. The apparatus of Claim 15 wherein said optical assembly includes a prism having a first surface and the biochip, and the prism and the biochip are assembled such that the surface of the biochip on which the spots reside is the only TIR surface of the optical assembly in the path of the beam of light.

25 **Claim 18.** The apparatus of Claim 17 wherein the biochip resides on a surface of the prism with an index matching fluid between them to cause polarized light to pass from the prism through the slide to the TIR surface and to be reflected back into the prism in a single reflection at the TIR surface and thereafter to exit the optical assembly

Claim 19. A method for obtaining spatially resolved images of a plurality of
30 spots of an array of spots on s biochip surface comprising;

placing a biochip having an array of spots on its upper surface into combination with a prism to form an optical assembly in which the upper surface of the biochip is a TIR surface and such that an extended beam of polarized light introduced into the optical assembly will have only a single reflection at the TIR surface.

5 **Claim 20.** The method of Claim 19 further comprising recording the spatially resolved images of spots on the biochip surface within the beam of light.

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